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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,913	03/01/2002	Maria De Lourdes Higuchi	A33474-PCT-USA-A - 068528	1698

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EXAMINER	
MONSHIPOURI, MARYAM	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,913	HIGUCHI ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received, or are present in the case.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *filed 12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's response to restriction requirement filed 11/8/2004 is acknowledged. Applicant elected Group IV invention (claims 11-15) without traverse. Claims 1-15 are canceled. Claims 16-21 are added.

DETAILED ACTION

Claims 16-21 are under examination on the merits.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on two applications filed in Brazil on 7/3/2000, namely PI 0002989-0 and PI 0102648-8. It is noted, however, that certified copies of said applications as required by 35 U.S.C. 119(b), are not of record in the case. Applicant is requested to provide said documents in response to this office action.

Also, it is noted that in the preliminary amendment of 3/1/2001 applicant has provided the priority information inserted underneath the title. However, said information is incomplete. Applicant is advised to complete said information in response to this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 16 and its dependent claims 17-18 and 21 are directed to a **genus** of agents from all sources and species (both synthetic and natural) that inhibit sialic acid mediated attachment of mycoplasma to cells that has not been adequately described in the specification.

The court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. " A written description of an invention involving chemical genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that " in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula fro others and can identify many of the species that the claims encompass. accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus". Here, the term "agent" in claim 16 is merely defined by function. The specification fails to fully disclose all the structural requirements of agents (both

synthetic and natural) that are comprised within the claimed genus. All applicant provides is **two species** namely antibiotics and neuraminidase/trans-silaidase enzymes which are insufficient to describe the structure of entire genus.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 16-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of use of antibiotics and active neuramindisae/trans-silaidase enzymes from T.cruzi for inhibiting sialic-acid mediated mycoplasma attachment to cells in the subject, does not reasonably provide enablement for method of use of all agents from all sources and species (both natural and synthetic) for inhibiting or preventing mycoplasma infection. Claim 16 is currently drawn to a method of treatment of mycoplasma infection utilizing agents (both natural and synthetic) from all sources and species that both inhibit and prevent sialic acid-mediated attachment of mycoplasma to cells in the subject.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2n 1400 (Fed. Cir. 1988) are: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

The specification fails to teach the structural requirements and in vivo properties (i.e. toxicity etc) of all agents that can be utilized in the method of claim 16, beyond those structures corresponding to antibiotics and enzymes from T.cruzi and how said gents could be targeted to the diseased cell or organ in the subject etc. No examples of such agents are provided either. Current state of the art is unpredictable as to what inhibitor agents may successfully be used in treating mycoplasma infection.

Therefore due to lack of sufficient teachings and examples about the structural and physiological properties of agents that may be utilized in the claimed invention and due to unpredictability of the art in terms of structural and physiological requiems of agents that may be successfully utilized in said method one of skill in the art has to go through the burden of undue experimentation in order to screen for those agents that are within the scope of the invention and as such claim 16 and its dependent claim 21 are not enabled. Claims 17-18 are subject to the scope of enablement rejection for not specifying the source and structure of neuraminidase and trans-sialidase enzymes as the specification fails to teach whether all trans-sialidase and neuraminidase from all sources may be successfully used in inhibiting trans-sialidase activity. With respect to claim 19, applicant is reminded even though is said claim the source of Trans-silalidase is specified, Uemura et al. (EMBO J. 11(11), 3837-3844, 1992, cited in the IDS) teaches that many trans-silaidase genes from T. Cruzi with structures very similar to SEQ ID NO:2, do not express prpducts that exhibit activity (see abstract). Therefore, in the absence of a clear structural information about claimed enzyme the invention is subject to scope of enablement rejection.

With respect to the term "prevent" in claim 16, applicant is reminded that neither the prior art nor the present disclosure provides any information about methods of preventing mycoplsma infection and thereby cancer by administering inhibitors (including trans-silaidase of T. cruzi). All the information and data provided in the disclosure indicates reduction or inhibition of mycoplasma infection and not its total prevention. Hence, considering *re Wands* factors above due to lack of sufficient examples and information provided about agents which totally prevent mycoplasma infection and due to unpredictability of prior art as to which agent result in total prevention of mycoplasma infection in patents one of skill in the art has to go through the burden of undue experimentation in order to prevent cancer caused by mycoplasma infection and as such claim 16 and its dependent claims 17-21 are subject to total lack of enablement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler et al. (Infect. and Immun., 38(2), 598-603, 1982, cited in the IDS) Feng et al. (Mol. Cell. Biol., 19(12), 7995-8002, 1999, cited in the IDS) in view of. Chandler teaches that *Mycoplasma pneumoniae* (*M. pnumoniae*) attachment to human intestinal carcinoma cell cultures (WiDr) occurs on neuraminidase sensitive, silaic acid containing

glycoporteins (see page 598). Chandler also teaches a method of inhibiting mycoplasma binding to WiDr cells "in vitro" or "in situ" , comprising preincubating said cells with sialoglycoproteins and gangliosides thereby saturating the mycoplamsa surface proteins with sialate residues from said products before exposing WiDr receptor cells to mycoplasma (see Table 3).

Chandler does not teach methods of treating undesirable cell proliferation associated with mycoplasma infection in a subject, utilizing agents that inhibit sialic-acid mediated attachment of mycoplasma to cells of the subject.

Feng teaches that chronic infection by mycoplasma induces chromosomal instability as well as malignant transformation of mammalian cells (see page 7995).

At the time the invention was made it would have been obvious to one of ordinary skill in the art to start with the "in vitro" method of Chandler and administer the sialoglycoproteins or gangliosides (listed in Table 3) in humans in order to treat malignant transformation of mammalian cells such as colon, prostate, lung etc. as taught by Feng. One of ordinary skill in the art is motivated in administering said sialoglycoproteins and gangliosides to patients because such products would reduce mycoplasma infection and its associated cell proliferation, in said patients and have potential be used as drugs against a variety of cancers in humans and mammals caused by mycoplasma infection.

Finally, one of ordinary skill in the art has a reasonable expectation of success in administering such gangliosides or sialoglycoproteins (products) to mammalian subjects

because said products are non-toxic and well established in terms of structure and organ targeting properties in the prior art, rendering the invention obvious.

Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler (cited above) in view of Feng further in view of Uemura et al. (EMBO J., 11(11), 3837-3844, 1992, cited in the IDS). As mentioned above, Chandler in view of Feng teaches a method of treating undesirable cell proliferation associated with mycoplasma infection comprising administering gangliosides and sialoglycoproteins, which inhibit sialic-mediated attachment of mycoplasma to the cells in subjects.

Chandler in view of Feng does not teach a method of inhibiting mycoplasma binding and infection comprising administering to a subject neuraminidase and/or trans-sialidase enzymes from T. cruzi.

Uemura teaches cloning isolation and purification of many trans-sialidases from T.cruzi, one of which having both said activities simultaneously, in the same enzyme.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the method of Chandler in view of Feng and replace the inhibitor agent (namely sialoglycoproteins and gangliosides) with the active T. cruzi trans-sialidase of Uemura. One of ordinary skill in the art is motivated is replacing the sialoglycoproteins of Chandler in view of Feng with the enzyme of Uemura because said enzyme will successfully remove the sialate residues on the host cell receptors and will transfer them to some other miscellaneous proteins in the blood or tissues, such that said residues will be totally unavailable and inaccessible for mycoplasma binding and infection on the surface of host cells.

One of ordinary skill in the art is motivated in replacing the inhibitor agent of Chandler in view of Feng with that of Uemura because T. cruzi trans-sialidase has both neuraminidase and trans-sialidase activities is a single enzyme and is expected to result in more inhibition than those provided by sialoglycoproteins of Chandler in view Feng.

Finally, one of ordinary skill in the art has a reasonable expectation of success in replacing the agents of Chandler in view of Feng with that of Uemura because once again methods of administering enzymes to mammalian organs are well established in the prior art, rendering the invention obvious.

Allowable Subject Matter

SEQ ID NO:2 is allowed. This is because SEQ ID NO:2 is free of prior art. Further the prior art does not teach or suggest preparing such specifically claimed product. Hence said sequence is also non-obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 or (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Mosnhipouri

Maryam Mosnhipouri Ph.D.

Primary Examiner

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